ENCAPSULATION OF FLUTICASONE PROPIONATE AND SALMETEROL XINAFOATE IN MICROPARTICLES OF CHITOSAN DERIVATIVE FOR COPD TREATMENT

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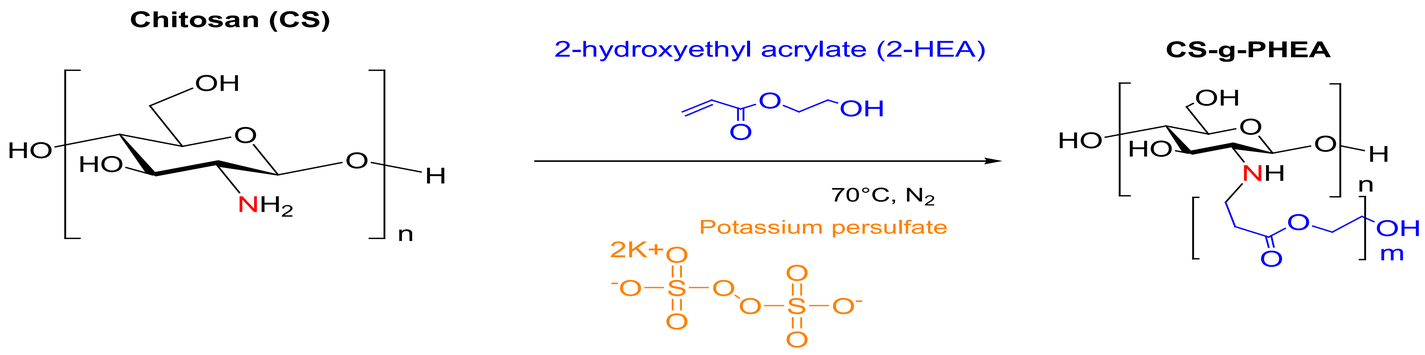
INTRODUCTION

- **Chronic obstructive pulmonary disease** (COPD) is associated with an enhanced chronic inflammation of the airways caused by tobacco smoking, air pollution or genetic factors
- **Fluticasone propionate** (FLU): corticosteroid with high topical activity
- **Salmeterol xinafoate** (SX): long-acting selective β_2-adrenoceptor agonist
- FLU and SX
  - √ Used in COPD treatment
  - × ***High degree of crystallinity, hydrophobic compounds***.
- Inclusion of SX, FLU in polymeric microparticles results their amorphization
- **Chitosan**, a natural polysaccharide, along with its derivatives have been used for the inclusion of various pharmaceutical compounds in nano- and microparticles

EXPERIMENTAL

→ *Modification of CS with 2-hydroxyethyl acrylate (2-HEA) through a free radical reaction*



→ *Encapsulation of Salmeterol Xinafoate (SX) and Fluticasone propionate (FLU) in CS-g-PHEA microparticles through ionic gelation technique. FLU and SX (Fig. 1 a, b) were simultaneously enclosed in their interior in 10, 20 and 30% ratios.*

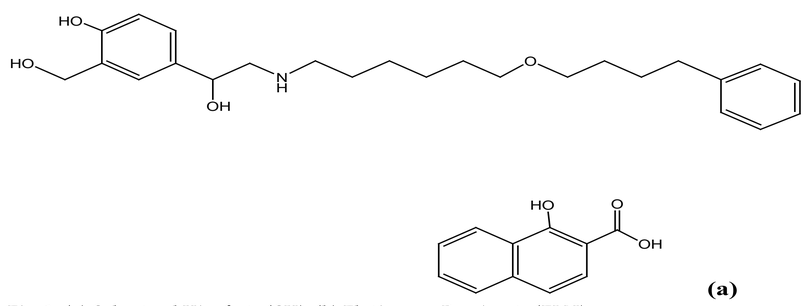


Fig. 1. (a) Salmeterol Xinafoate (SX), (b) Fluticasone Propionate (FLU)

RESULTS & DISCUSSION

FTIR

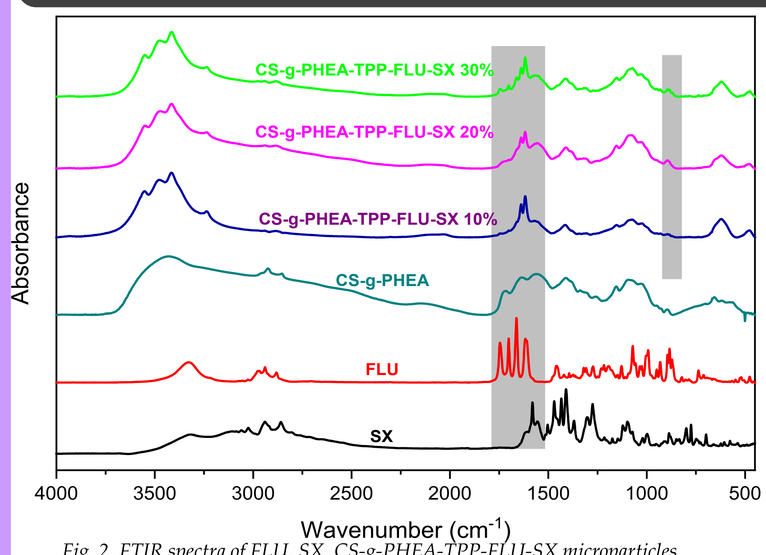


Fig. 2. FTIR spectra of FLU, SX, CS-g-PHEA-TPP-FLU-SX microparticles

Characteristic FLU IR bands:
- 1024 cm^{-1} C-F stretch
- 1452 cm^{-1} -OH bend
- 1715 cm^{-1} >C=O stretch

Characteristic SX IR bands:
- 1409cm^{-1} -OH bend
- 1580cm^{-1} >N-H bend

Interactions between drugs and polymeric material → **Successful inclusion** of FLU and SX in CS-g-PHEA microparticles (Fig.2).

XRD

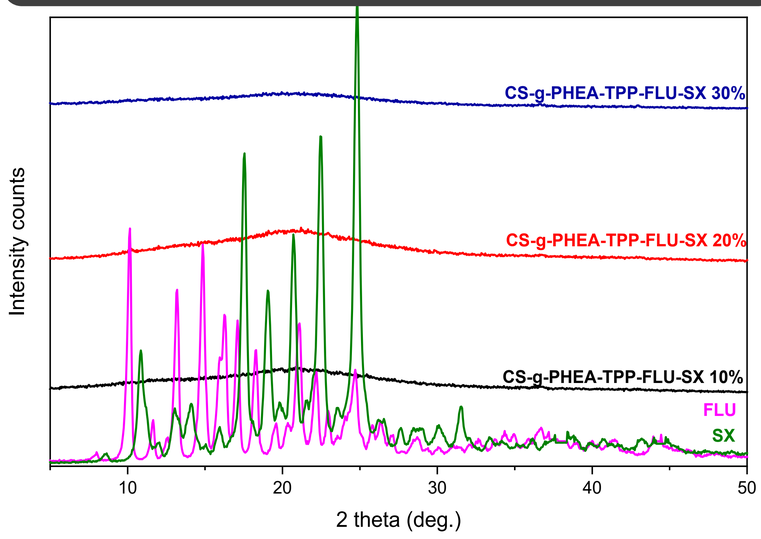


Fig. 3. XRD of FLU, SX, CS-g-PHEA-TPP-FLU-SX microparticles

Inclusion of FLU and SX in CS-g-PHEA microparticles affects the crystallinity of the drugs → **FLU and SX amorphization** (Fig. 3).

SEM & DLS

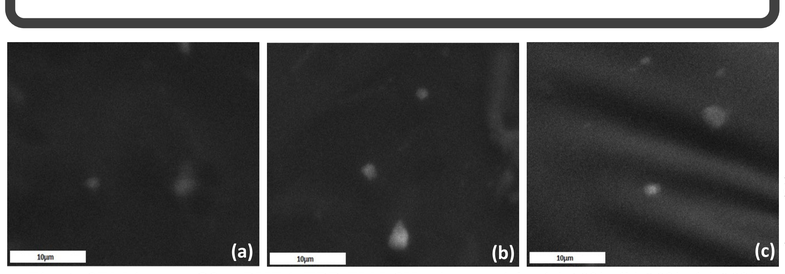


Fig. 4. SEM images CS-g-PHEA-TPP-FLU-SX microparticles (a) 10%, (b) 20%, (c) 30%

Fig 4. (a-c) and Table 1. confirm the successful preparation of **spherical shaped individual micro-scaled particles**

Table. 1. Size (nm) of CS-g-HEA- FLU-SX microparticles

Sample	Z-Average (d.nm)	Zeta Potential (mV)
CS-g-PHEA-TPP-10% FLU/SX	754	+26.7
CS-g-PHEA-TPP-20% FLU/SX	1005	+22.6
CS-g-PHEA-TPP-30% FLU/SX	2216	+26.6

In Vitro RELEASE

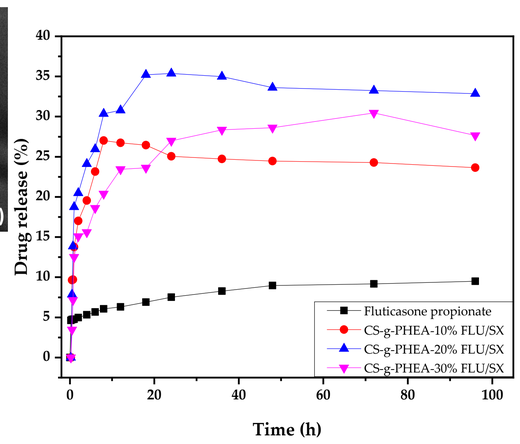


Fig. 6. *In vitro release for different loading capacities of FLU from CS-g-PHEA microparticles*

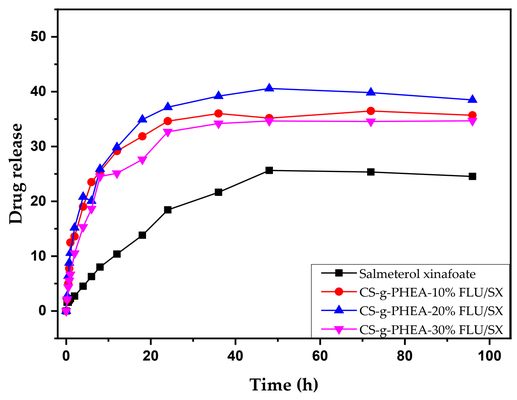


Fig. 5. *In vitro release for different loading capacities of SX from CS-g-PHEA microparticles*

In vitro dissolution test of CS-g-PHEA microparticles in simulated body fluids (Fig 5 and 6).
- ✓ Sustained release of SX and FLU
- ✓ Enhancement of FLU and SX release up to 35 % and 40 % respectively

CONCLUSIONS

- ✓ *Modified chitosan microparticles were synthesized* and FLU and SX were successfully incorporated in their interior.
- ✓ FT-IR spectroscopy evaluated the CS-g-PHEA-FLU-SX interactions, confirm a *successful inclusion*.
- ✓ XRD analysis showed the *amorphization of FLU and SX* into the microparticles.
- ✓ The prepared microparticles were of *spherical shape*, in micro scale.
- ✓ *Sustained* and *enhanced release* of SX and FLU was achieved

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